

Case Report
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A Case Report of Mammary Analogue Secretory Carcinoma with Aggressive Clinical and Histological Presentation

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ABSTRACT

Mammary analogue secretory carcinoma is a rare salivary gland tumor that has a wide range of clinical presentation ranging from indolent, local and slowly growing tumors to a very aggressive, infiltrative and widely metastasizing forms.

We report a case of an unfortunate patient whose tumor had a very quick ominous disease course with aggressive clinical and histological presentation. This case is the first case, to our knowledge, to be reported in the literature from Saudi Arabia of MASC with features of high grade transformation.

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Introduction

Mammary analog secretory carcinoma (MASC) was described early in 2010 by Skálová et al. It is a rare salivary gland tumor that shares a lot of morphological and cytogenetic features with a unique breast carcinoma of children and young adults, the secretory carcinoma [1]. The major similarity between MASC and secretory carcinoma of the breast is the presence of the translocation t(12;15) (p13;q25), that results in the formation of the oncogenic fusion gene ETV6-NTK [5,6], this translocation is also seen in other tumors such as infantile fibrosarcoma congenital mesoblastic nephroma and myelogenous leukemia [7]. MASC is another salivary gland tumor that has breast tumor analog, beside mucoepidermoid carcinoma, acinic cell carcinoma and pleomorphic adenoma [11]. Recently few cases with aggressive clinical behavior have been reported and they seemed to show more bizarre and high grade histological morphology changes than what used to be described.

Case presentation

A 79 years old gentleman presented to the ENT clinic in January 2018 with a large non-tender submental mass, measuring 4x4x3cm which was increasing in size over the past four months.

An excisional biopsy was taken and during the operation, wherein the surgeon stated that the tumor was infiltrative to the surrounding neck structures and complete excision was not feasible.

Frozen section examination confirmed the malignant neoplastic process by showing sheets of pleomorphic cells with abundant vacuolated cytoplasm and scattered extracellular dense eosinophilic

material. [Figure 1]

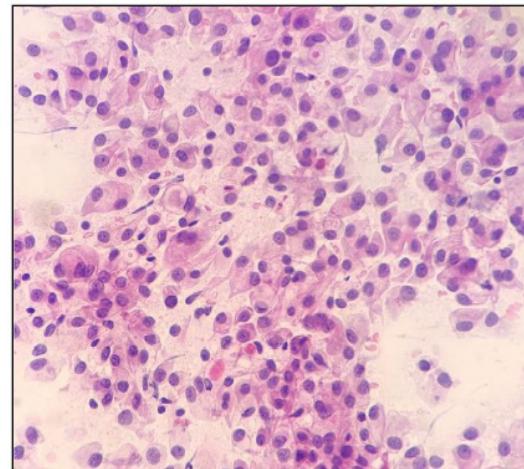


Figure 1: Frozen section slide showing sheets of the malignant cells with vacuolated cytoplasm and scattered extracellular dense eosinophilic colloid-like material.

Histological examination later on showed cohesive sheets of intermediate sized cells with eosinophilic/amphophilic vacuolated cytoplasm with low grade, bland nuclei and prominent nucleoli. The neoplasm grew in solid, trabecular and microcystic patterns. [Figure 2] It contained areas of intracellular and extracellular -PAS and alcian blue positive colloid-like material with bubbly appearance. [Figure 3]

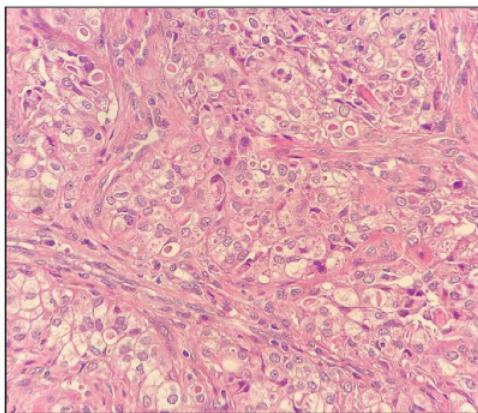


Figure 2: Tumor grew in solid, trabecular and microcystic patterns with colloid-like material.

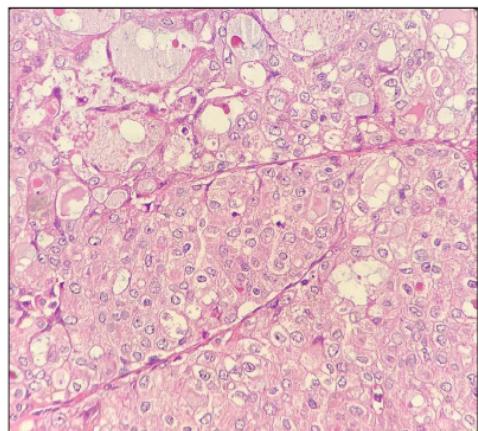


Figure 3: Tumor showed extracellular -PAS and alcian blue positive material with bubbly appearance.

In addition to that, the tumor exhibited histological signs of high grade transformation as scattered large atypical cells with bizarre irregular hyperchromatic nuclei, with increased mitotic figures. The proliferating index of the tumor (Ki-67) was more than 40%. The tumor infiltrated the surrounding skeletal muscles and fat. Areas of extensive perineural invasion and necrosis were also present. [Figures 4 and 5]

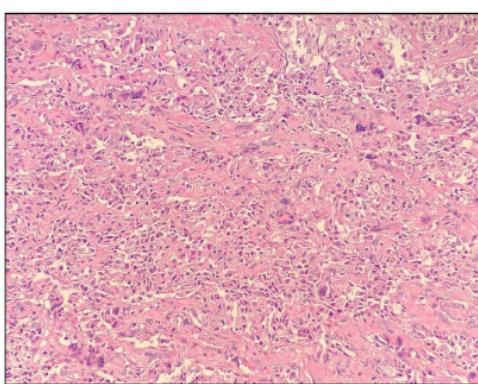


Figure 4: Tumor showed scattered large cells with bizarre nuclei.

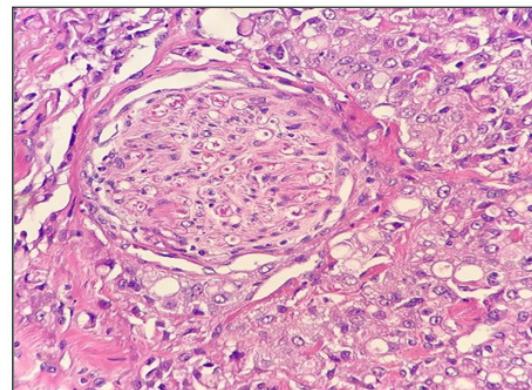


Figure 5a: Perineural invasion by tumor cells

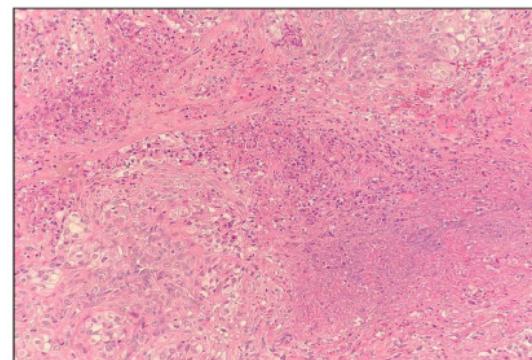


Figure 5b: Extensive areas of coagulative necrosis

Immunohistochemistry stains showed that tumor cells were strongly positive for Mammaglobin, S-100, CK7, CK5/6 and GCDFP-15. Cytogenetics testing by FISH analysis of the tumor confirmed presence of chromosomal translocation $t(12;15)$ (p13;q25), gene rearrangements on ETV6 gene from chromosome 12 and the NTRK3 gene from chromosome 15.

Two weeks after the diagnosis was established the patient complained of shortness of breath and coughing. CT chest showed multiple metastatic lung nodules and moderate pleural effusion. Cytological examination of the pleural fluid confirmed the presence of metastatic nodules to his lungs as well as liver. [Figure 6] The patient unfortunately died three months after his first presentation.

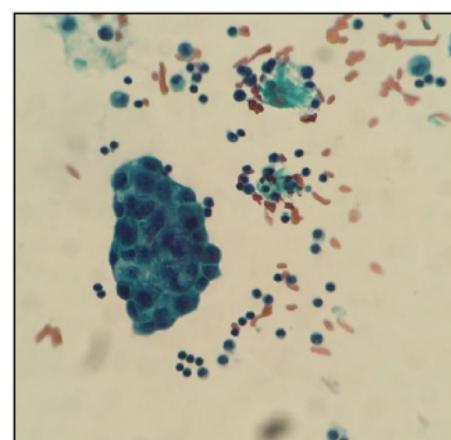


Figure 6: Pleural effusion cytology smear showing small cohesive balls of malignant cells with bubbly cytoplasm

Discussion

MASC predominantly affects men more than women and often behave in an indolent nature [2,3]. The parotid gland is the most common affected gland but few cases were also seen in the submandibular glands [4].

Histologically the tumor shows variable patterns of growth such as solid, microcystic, tubular, papillary, and cribriform patterns. The cells often are of low grade morphology with uniform cells, small- to medium-sized nuclei, occasional small nucleoli, and abundant pink, bubbly cytoplasm. Mitotic figures are usually rare [8]. Characteristically seen in MASC is the extracellular mucin-like and/or eosinophilic colloid-like material. When the tumor shows areas of “dedifferentiation” /high grade transformation, one can see extracapsular/extraglandular extension and perineural invasion. [9] As well as marked cellular and nuclear atypia, solid and microcystic growth pattern, and areas of extensive necrosis [10].

For confirming the diagnosis of MASC, the utility of ETV6 rearrangement by FISH comes superior to immunohistochemistry stains due to the high specificity of the test. Most of the immunohistochemistry stains that are positive in MASC show overlap with other salivary gland tumors. In a study done at the Johns Hopkins Hospital in 2013 and included over 155 salivary gland neoplasms of different types, all 15 MASCs were positive for the ETV6 rearrangement by FISH but it was not identified in any of the other types of salivary gland tumors (100% vs. 0%, $p < .0001$, Fischer's exact). [12] All cases of MASC were immunoreactive for mammoglobin, but also cases of low-grade cribriform cystadenocarcinoma, polymorphous low-grade adenocarcinomas, salivary duct carcinomas, mucoepidermoid carcinomas, and few cases of pleomorphic adenomas which did not harbor the ETV6 rearrangement showed mild to moderate reactivity [12].

MASC are usually positive for S-100, vimentin, HMWK, CK7, GCDFP, CAM5.2, CK19, MUC1 and MUC4.

In summary immunohistochemistry can help support the diagnosis of MASC, however the gold standard method for its diagnosis is FISH analysis for ETV6 rearrangement.

Survival and treatment

MASC is considered a low-grade carcinoma with a favorable prognosis that infrequently recur after surgical resection, so treatment should mimic the usual management of other low-grade malignant salivary gland neoplasms. However when high-grade transformation occurs, a more aggressive multidisciplinary management should be considered because of its poor prognosis.

The inhibition of ETV6-NTRK3 gene fusion could be used as treatment in the future, and this is a topic of discussion and research in the current time.

Conclusion

MASC is a neoplasm that is newly recognized and its clinical behavior cannot be predicted. Reporting and studying many cases are needed for better understanding. Therefore, we encourage pathologists to do pathology review of cases previously diagnosed at their institutes as other types of salivary gland tumors that have suspicious histology for MASC or unclassical features for what they have been diagnosed with by testing for MASC specific gene rearrangement. Such studies might reveal more cases of MASC

in Saudi Arabia which can help in future studies and achieving better understanding of this unique tumor.

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